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Ferrous Fumarate and Docusate Sodium Extended-Release Tablets

» Ferrous Fumarate and Docusate Sodium Extended-Release Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of ferrous fumarate ($C_4H_2FeO_4$) and not less than 90.0 percent and not more than 115.0 percent of the labeled amount of docusate sodium ($C_{20}H_{37}NaO_7S$).

Packaging and storage—Preserve in well-closed containers.

Labeling—Label the Tablets in terms of the content of ferrous fumarate ($C_4H_2FeO_4$) and in terms of the content of elemental iron.

USP Reference standards ⟨11⟩—
USP Docusate Sodium RS

Dissolution ⟨711⟩—
Medium: 0.1 N hydrochloric acid; 900 mL.
Apparatus 2: 50 rpm.
Times: 1 and 3 hours.
Determine the amount of Fe (II) dissolved, on filtered portions of the solution under test, employing the method described under *Assay for ferrous fumarate* with the following modification.
Standard solution—Transfer the appropriate amount of *Iron stock solution* to a volumetric flask, and dilute with 0.1 N hydrochloric acid in such a way that the final concentration is similar to that expected in the solution under test.
Tolerances—The percentages of the labeled amount of Fe (II) dissolved at the times specified conform to *Acceptance Table 2.*

Time (hours)	Amount dissolved
1	between 40% and 75%
3	not less than 80%

Uniformity of dosage units ⟨905⟩**:** meet the requirements with respect to iron.

Assay for ferrous fumarate—
6 N Hydrochloric acid—Slowly add 5 mL of hydrochloric acid to 5 mL of water, and mix.
Diluting solution—Add 1 mL of *6 N Hydrochloric acid* to 59 mL of water, and mix.
Phosphoric acid solution—Dilute 20 mL of phosphoric acid with *Diluting solution* to 200 mL, and mix.
Iron stock solution—Transfer about 350 mg of ferrous ammonium sulfate hexahydrate, accurately weighed, to a 1000-mL volumetric flask, dissolve in *Diluting solution,* dilute with *Diluting solution* to volume, and mix to obtain a solution having a known concentration of about 50 µg per mL.
Standard preparations—To separate 100-mL volumetric flasks transfer 2.0, 4.0, 6.0, 8.0, and 10.0 mL of *Iron stock solution.* To each flask add 6.0 mL of *Phosphoric acid solution,* dilute with *Diluting solution* to volume, and mix. The *Standard preparations* so obtained contain about 1.0, 2.0, 3.0, 4.0, and 5.0 µg of iron per mL, respectively.
Blank solution—Transfer 6.0 mL of *Phosphoric acid solution* to a 100-mL volumetric flask, dilute with *Diluting solution* to volume, and mix.
Assay preparation—Weigh and finely powder not fewer than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 1.5 g of ferrous fumarate, to a 1000-mL volumetric flask, add 110 mL of *6 N Hydrochloric acid,* and boil for 30 minutes. Cool, dilute with water to volume, mix, and filter. Transfer 5.0 mL of this solution to a 50-mL volumetric flask, dilute with *Diluting solution* to volume, and mix. Transfer 8.0 mL of this solution to a 100-mL volumetric flask, add 6.0 mL of *Phosphoric acid solution,* dilute with *Diluting solution* to volume, and mix to obtain a solution having a known concentration of about 4 µg of iron per mL.
Procedure—Concomitantly determine the absorbances of the *Standard preparations* and the *Assay preparation* at the iron emission line at 248.3 nm with a suitable atomic absorption spectrophotometer (see *Atomic Absorption Spectroscopy* ⟨852⟩) equipped with an iron hollow-cathode lamp and an air–acetylene flame, using the *Blank solution* as the blank. Plot the absorbances of the *Standard preparations* versus their concentrations, in µg per mL, of iron, and draw the straight line best fitting the five plotted points. From the graph so obtained, determine

the concentration, in µg per mL, of iron in the *Assay preparation.* Calculate the average quantity, in mg, of ferrous fumarate ($C_4H_2FeO_4$) in each Tablet taken by the formula:

$$(TC/D)(169.90/55.85)$$

in which *T* is the labeled quantity, in mg, of ferrous fumarate in each Tablet; *C* is the concentration, in µg per mL, of iron in the *Assay preparation; D* is the concentration, in µg per mL, of ferrous fumarate in the *Assay preparation,* based on the labeled quantity per Tablet and the extent of dilution; and 169.90 and 55.85 are the molecular weight of ferrous fumarate and the atomic weight of iron, respectively.

Assay for docusate sodium—

Calcium acetate solution—Dissolve 4 g of calcium acetate in 2000 mL of water.

Diluting solution—Mix 450 mL of acetonitrile and 550 mL of *Calcium acetate solution.*

Mobile phase—Add 2 mL of phosphoric acid to 1000 mL of *Diluting solution,* and mix. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩). Filter, and degas.

Standard preparation—Dissolve an accurately weighed quantity of USP Docusate Sodium RS in *Diluting solution* to obtain a solution having a known concentration of about 1 mg per mL.

Sodium benzoate solution—Dissolve an accurately weighed quantity of sodium benzoate in *Diluting solution,* and dilute quantitatively and stepwise with the same solvent to obtain a solution having a known concentration of about 8 µg per mL.

Resolution solution—Dissolve a suitable quantity of USP Docusate Sodium RS in *Sodium benzoate solution* to obtain a solution containing about 1 mg per mL of docusate sodium.

Assay preparation—Transfer a number of Tablets, equivalent to about 2 g of docusate sodium, to a 2000-mL volumetric flask. Add about 1500 mL of *Diluting solution,* and sonicate with frequent shaking until the Tablets are completely disintegrated. Cool, dilute with *Diluting solution* to volume, and mix. Centrifuge, and use the clear supernatant. If the supernatant is not clear, pass through a membrane filter.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 214-nm detector and a 4.6-mm × 30-cm column that contains 3-µm packing L1. The flow rate is about 1.5 mL per minute. Chromatograph the *Resolution solution* and the *Standard preparation,* and record the peak responses as directed for *Procedure:* the resolution, *R,* between sodium benzoate and docusate sodium is not less than 7.0; the tailing factor is not less than 0.9 and not more than 3.5; the column efficiency is not less than 1000 theoretical plates; and the relative standard deviation for six replicate injections of the *Standard preparation* is not more than 2.0%. The relative retention times are 1.0 for docusate sodium and 0.25 for sodium benzoate.

Procedure—Separately inject equal volumes (about 25 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the average quantity, in mg, of docusate sodium ($C_{20}H_{37}NaO_7S$) in each of the Tablets taken by the formula:

$$(2000C/N)(r_U/r_S)$$

in which *C* is the concentration, in mg per mL, of USP Docusate Sodium RS in the *Standard preparation; N* is the number of Tablets taken; and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
FERROUS FUMARATE AND DOCUSATE SODIUM EXTENDED-RELEASE TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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